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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,779	09/28/2007	Michael Teifel	40695.00600	9429

38647 7590 04/22/2011

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EXAMINER	
SCHULTZ, JAMES	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
04/22/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,779	TEIFEL ET AL.	
	Examiner	Art Unit	
	James D. (Doug) Schultz	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-77* is/are pending in the application.

4a) Of the above claim(s) *64-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-63 and 67-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's responses filed August 8, 2010 and January 18, 2011 have been considered. Rejections and/or objections not reiterated from the previous office action mailed April 8, 2010 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicants' election of the species "pancreatic cancer" as a species of cancer, and the further election of the species "paclitaxel" as the species of active agent is acknowledged. By way of clarification, it is noted that there are 6 independent claims (i.e. claims 36, 44, 52, 55, 57, and 70), some of which have been amended to now recite varying combinations of "paclitaxel", and/or an "active agent", and/or a "further active agent". Since this may cause substantial confusion, it is worth attempting a clarification at the outset as to what the election of the species "paclitaxel" is actually considered to refer to given the frequent and variable use of the term "active agent" in the claims. Looking at the restriction requirement of July 24, 2009, the examiner required election of a single species of "active agent" as recited in claim 24 and 26-31. It seems apparent that the species election applied to both the "active agent" as well as the "further active agent", since claims 24 and 26-31 recite both independently. See restriction requirement of July 24, 2009, page 3 last paragraph. In the response to this restriction requirement dated December 23, 2009, applicants canceled all original claims and indicated that

canceled claims 24 and 26-31 correspond to newly pending claims 59 and 61-66. Claims 59 and 61 depend ultimately from independent claims 52 and 55, respectively. Claims 52 and 55 recite both "paclitaxel" and "an active agent". It is not clear if paclitaxel and the active agent are necessarily the same reagent in these claims. Claims 62 and 63 both ultimately depend from claim 44, which recites paclitaxel, and a "further active agent". Accordingly, in reference to the election of species, since paclitaxel was explicitly recited in the claims at the time applicants were required to elect an active agent, and since applicants elected at that time the species paclitaxel, paclitaxel is considered to comprise the elected active agents recited in any of the instantly pending claims (whether it is referred to as an “active agent”, or “further active agent”). Furthermore, at least claims 52, 55 and 57 are rejected as being indefinite given the unclear relationship between paclitaxel and the active agents recited in these claims. This last matter is explained further below.

Applicants have traversed the election of species because it is alleged that the search for one species of cancer or chemotherapeutic agent will give results that are relevant to the search for other species of cancer or chemotherapeutic agent. This is not considered convincing, because this is not considered necessarily true. Applicants have provided no evidence that the search for treatments of breast cancer is (for example) commensurate in scope or would even be capable of supplying relevant art against the same treatment directed towards prostate cancer, for example. In the lack of such evidence, the assertion that a search for one would provide results relevant to another is considered mere attorney argument, which may not take the place of evidence or reasoning. Furthermore, there is also an additional examination burden as the state of the art for treating an breast cancer (for example) is considered to be different from the state of

the art of treating prostate cancer, for example, and thus their respective analyses for enablement and written description are also different. Finally, applicants are reminded that this application was filed under 35 USC § 371, and under the rules of lack of unity which pertain thereto, there is no provision for search burden. The requirement for an election of species is considered proper, and is maintained therefore.

Applicants have included claim 56 on the list of claims that the elected species read on because it is alleged that pancreatic cancer may metastasize to the liver. Accordingly, claim 56 is examined herein insofar as claim 56 reads on pancreatic cancer that has metastasized to the liver.

This application contains claims 64-66, drawn to an invention nonelected with traverse in the reply filed on January 18, 2011. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 52-61, and 74-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As explained above, claims 52, 55, and 57 all recite both paclitaxel and an active agent, where it is unclear if the active agent is paclitaxel. For the purposes of interpreting these claims towards applying art, these terms are considered to be equal since there is nothing to contradict

this presumption on the record, and since the elected active agent is paclitaxel. However, the language as recited is considered vague and indefinite, and clarification is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36-63, and 67-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over McDonald (U. S. Patent Number 7,112,338) in view of Rahman et al. (U. S. Patent Number 6,146,659). This rejection is repeated for the same reasons of record as set forth in the action mailed April 6, 2010, but newly applied against newly submitted claims 71-77. The rejection is reproduced below, and responses to applicant's traversal follow.

Claim 36 recites a method of treating a patient suffering from a disease or condition comprising administering to a patient in need thereof a pharmaceutical composition at a monthly dose of about 0.25 mg up to about 60 mg of paclitaxel/kg body weight of the patient, wherein the pharmaceutical composition comprises a cationic liposomal preparation comprising at least one cationic lipid from about 30 mole% to about 99.9 mole%, paclitaxel in an amount of at least about 0.1 mole% and at least one neutral and/or anionic lipid from about 0 mole % to about 70 mole%. Claim 37 recites the method of claim 36, wherein the monthly dose is about 0.5 mg up to about 30 mg paclitaxel/kg body weight. Claim 38 recites the method of claim 37, wherein the monthly dose is about 1.0 mg up to about 15 mg paclitaxel/kg body weight. Claim 39 recites the

method of claim 37, wherein the monthly dose is about 1 to about 7.5 mg/paclitaxel/kg body weight. Claim 40 recites the method of claim 36, wherein the monthly dose is about 20 to about 60 mg/paclitaxel/kg body weight. Claim 41 recites the method of 36, wherein administering the cationic liposomal preparation comprises administering at least once daily. Claim 42 recites the method of claim 36, wherein administering the cationic liposomal preparation comprises administering a plurality of times during a month period, and wherein each administration is separated by an interval of between one day and 3 weeks. Claim 43 recites the method of claim 36, wherein administering the cationic liposomal preparation comprises administering (i) at least 3 times or 3-5 times in a first week, followed by an interval of 1-3 weeks without administration, and optionally one or several repeats of this protocol; (ii) once in a first week followed by an interval of at least one week or 1-3 weeks, without administration, and optionally one or several repeats of this protocol; (iii) once in a week for one week or several successive weeks; or (iv) a combination of (i), (ii) and/or (iii).

Claim 44 recites a method of treating a patient suffering from a disease or condition with a combination therapy comprising administering to a patient in need thereof a pharmaceutical composition comprising a cationic liposomal preparation comprising at least one cationic lipid from about 30 mole% to about 99.9 mole%, paclitaxel in an amount of at least about 0.1 mole% and at least one neutral and/or anionic lipid from about 0 mole % to about 70 mole%, wherein the composition is administered simultaneously, separately, or sequentially with an effective dose of at least one further active agent and/or heat and/or radiation and/or cryotherapy. Claim 45 recites the method of claim 44, wherein the composition is administered simultaneously with an effective dose of at least one further active agent. Claim 46 recites the method of claim 36,

wherein the cationic liposomal preparation comprises paclitaxel in an amount of at least about 2 mole% to about 8 mole%. Claim 47 recites the method of claim 36, wherein the cationic liposomal preparation comprises paclitaxel in an amount of about 2.5 mole% to about 3.5 mole%. Claim 48 recites the method of claim 36, wherein the cationic liposomal preparation comprises 50:47:3 mole% of DOTAP, DOPC and paclitaxel. Claim 49 recites the method of claim 36, wherein the cationic liposomal preparation comprises substantially no paclitaxel crystals. Claim 50 recites the method of claim 36, wherein the condition is an angiogenesis-associated condition. Claim 51 recites the method of claim 50, wherein the disease or condition is a wound healing, cancer, an inflammatory disease or a chronic inflammatory disease such as rheumatoid arthritis, dermatitis, psoriasis or endometriosis.

Claim 52 recites a method of treating or preventing a disorder associated with and/or accompanied by occurrence of drug resistant cells, such as drug resistant tumors comprising administering to a patient in need thereof a pharmaceutical composition comprising at least one cationic lipid from about 30 mole% to about 99.9 mole%, an active agent in an amount of at least about 0.1 mole% and at least one neutral and/or anionic lipid from about 0 mole % to about 70 mole%. Claim 53 recites the method of claim 52, wherein the method is a second or third line treatment for cancer. Claim 54 recites the method of claim 52, wherein the cationic liposomal preparation comprises 50:47:3 mole% of DOTAP, DOPC and paclitaxel.

Claim 55 recites a method of treating or preventing metastasis formation, such as an onset and/or progression, particularly associated with and/or accompanied by a tumor disorder comprising administering a pharmaceutical composition comprising a cationic liposomal preparation comprising at least one cationic lipid from about 30 mole% to about 99.9 mole%, an

active agent in an amount of at least about 0.1 mole% and at 1least one neutral and/or anionic lipid from about 0 mole % to about 70 mole%. Claim 56 recites the method of claim 55, wherein the method treats or prevents liver metastasis formation.

Claim 57 recites a method of treating a patient with a combination therapy comprising administering to a patient in need thereof a pharmaceutical composition comprising a cationic liposomal preparation comprising at least one cationic lipid from about 30 mole% to about 99.9 mole%, an active agent in an amount of at least about 0.1 mole% and at least one neutral and/or anionic lipid from about 0 mole % to about 70 mole% for manufacturing a pharmaceutical composition, wherein the composition is administered simultaneously, separately, or sequentially with an effective dose of at least one further active agent and/or heat and/or radiation and/or cryotherapy against metastasis onset and/or progression, e.g. associated with and/or accompanied by the tumors. Claim 58 recites the method of claim 57, wherein the composition is administered simultaneously with an effective dose of at least one further active agent. Claim 59 recites the method of claim 52, wherein the active agent is selected from a cytotoxic or cytostatic substance such as an anti-tumor or an anti-endothelial cell active substance, a chemotherapeutic agent or an immunological active substance. Claim 60 recites the method of claim 55, wherein the cationic liposomal preparation comprises 50:47:3 mole% of DOTAP, DOPC and paclitaxel. Claim 61 recites the method of claim 55, wherein the active agent is selected from a taxane, a camptothecin, a statin, a depsipeptide, thalidomide, other agents interacting with microtubuli such as discodermolide, laulimalide, isolaulimalide, eleutherobin, Sarcodictyin A and B, and in a most preferred embodiment it is selected from paclitaxel, docetaxel, camptothecin or any derivative thereof. Claim 62 recites the method of claim 44, wherein the further active agent is an

anti- endothelial cell active substance, an anti-tumor active substance, a chemotherapeutic agent, an immunological active substance, a compound that reduces or eliminates hypersensitivity reactions or a chemosensitizer. Claim 63 recites the method of claim 44, wherein the further active agent is selected from antineoplastic agents especially antimitotic agents like paclitaxel, alkylating agents especially platinum containing compounds like cisplatin, carboplatin, DNA topoisomerase inhibiting agents like camptothecin or doxorubicin, RNA / DNA antimetabolites, especially 5- fluorouracil or gemcitabine and other compounds having antitumor activity.

Claim 67 recites the method of claim 36 for the treatment of cancer, especially pancreatic cancer, inoperable pancreatic cancer, gastro-intestinal cancer, lung cancer, colorectal or gastric cancer, breast cancer, prostate cancer and melanoma. Claim 68 recites the method of claim 36, wherein the cationic liposomal preparation comprises liposomes having an average particle diameter from about 25 nm to about 500 nm, preferably about 100 nm to about 300 nm Claim 69 recites the method of claim 36, wherein the cationic liposomal preparation is administered systemically, preferably intravenously.

Claim 70 recites a method of treating a disease or condition comprising administering to a patient in need thereof a pharmaceutical composition at a monthly dose of about 9 mg up to about 2337 mg of paclitaxel/m2 body surface of the human patient, wherein the pharmaceutical composition comprises at least one cationic lipid from about 30 mole% to about 99.9 mole%, paclitaxel in an amount of at least about 0.1 mole% and at least one neutral and/or anionic lipid from about 0 mole % to about 70 mole%. New claims 71-77 limit the mole% of the neutral or anionic lipid to a range of between about 1 mole% to 70 mole%.

McDonald et al. teach the use of liposomally delivered paclitaxel for the purpose of treating cancer in a variety of %mole concentrations of cationic and neutral lipids that are within the range claimed instantly including the specifically claimed 50:47:3 ratio of DOTAP/DOPC/paclitaxel (see paragraph 82 and on, particularly paragraph 87 for example). McDonald teach the use of a variety of additional inhibitors of angiogenesis and chemotherapeutics that are to be used in conjunction with the paclitaxel liposomes of McDonald et al., and that such treatments constitute at least a second line of treatment (para. 93 for example). McDonald teach using paclitaxel in combination with other chemotherapeutics (para. 9). McDonald also teach such liposomes having a particle diameter that overlaps almost exclusively with the instant patent claims (Para. 64 for example).

McDonald do not teach the dosing frequency (i.e. daily, monthly etc) and the instantly claimed mg/kg body weight of paclitaxel, although paragraph 102 of McDonald states that

> "The amount of angiogenic inhibitor or promoter will depend upon the size, age, sex, weight, and condition of the patient as well as the potency of the substance being administered. Having indicated that there is considerable variability in terms of dosing, it is believed that those skilled in the art can, using the present disclosure, readily determine appropriate dosing by first administering extremely small amounts and incrementally increasing the dose until the desired results are obtained. Although the amount of the dose will vary greatly based on factors as described above, in general, the present invention makes it possible to administer substantially smaller amounts of any substance as compared with delivery systems which target the surrounding tissue e.g., target the tumor cells themselves.

Rahman et al. teach dosing ranges for liposomally encapsulated paclitaxel and teaches dosing may take place daily, weekly or monthly, and for how long.

It would have been obvious to one of ordinary skill in the art to develop a dosing regimen using the liposomal formulations of McDonald, which are identical to those claimed, but

experimenting in a manner suggested by both McDonald and Rahman to achieve the instantly claimed schedules and doses. In the absence of evidence to the contrary, one of ordinary skill in the art would have to do no more than perform routine optimization of the regimens taught by the cited prior art to arrive at the instantly claimed invention. ""[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)". (see M.P.E.P. 2144.05). Accordingly, in the absence of evidence to the contrary, one of ordinary skill in the art would have considered the claimed invention to have been prima facie obvious at the time of filing.

Response to arguments

Applicants traverse the instant rejection by arguing that Rahman relates to the problem of administering paclitaxel in a rapid and less toxic schedule (col. 2, lines. 34-38), and that Rahman is "completely silent on the problem of providing a therapeutically effective schedule for the administration of paclitaxel"(applicants arguments response of February 22, 2011, page 8), and conclude that "one skilled in the art does not obtain any information from Rahman that would enable him to administer liposomes comprising paclitaxel with a predictable effectiveness.

In response, it is respectfully submitted that applicants position that Rahman is completely silent on the problem of providing a therapeutically effective schedule for the administration of paclitaxel is simply in error. In fact, the background section of Rahman discusses in some depth no less than six prior art publications, each of which are concerned with

dosing regimens and schedules of liposomally administered paclitaxel, and begins the very next section ("Summary of the in Invention") as follows:

> "The present invention provides a method of administering a taxane to a patient by administering taxane over a period of less than an hour in an amount from about 75 to 300 mg/m.sup.2 wherein the taxane is a liposomal encapsulated taxane or an antineoplastic derivative thereof..."

Accordingly, and contrary to applicants express statements, it is considered more reasonable to conclude that Rahman is solely concerned with therapeutically effective dosing schedules. In fact, the examiner is challenged to locate any passage from Rahman that does not at least peripherally relate to determining and describing liposomal administration of paclitaxel. This argument is considered unconvincing.

Applicants argue that "McDonald only relates to liposomal compositions comprising paclitaxel." Applicants also allege that "McDonald does not provide any relevant teaching on how to administer the disclosed to liposomal compositions with predictable safety and effectiveness (emphasis in original; applicant's arguments, supra). Respectfully, McDonald does not relate "only to liposomal compositions comprising paclitaxel." In fact, paragraph 102 of McDonald (cited above in the originally stated rejection) discusses how to determine how much liposomally encapsulated paclitaxel to administer, how to determine a patient population, and how to determine the concentration of paclitaxel to use. Clearly, McDonald does more than simply discussing compositions. While applicants have argued that this passage is a "generic trial and error method of finding a suitable dosing for a drug without undue experimentation", at a minimum it nevertheless directly contradicts applicants express statement that McDonald "only relates" to compositions.

More compelling is applicants arguments that McDonald does not direct or suggest to one skilled in the art the dosing schedule of the claimed invention. Both Rahman and McDonald (independently) teach the exact liposome as claimed. In fact, the only difference between the teachings of either of Rahman or McDonald and the instant claims is the concentration of paclitaxel to be delivered over a specified time period. Before considering these arguments in further depth, applicants' attention is directed to the breadth of the dosing schedules required in their claims, which is considered to be very broad, varying from 0.25 mg up to about 60 mg of paclitaxel per kilogram of body weight per month. Compare this to Rahman, who discloses at column 4:

> "The present pharmaceutical composition is administered in the amount of about 50 to 300 mg active compound/m^2 of mammalian host surface area. **For a human, for example, of about 70 kg body weight, from about 0.5 to 5.0 mg active compound per kg of body weight is administered.** Preferably, about 1.0-3.0 mg of active compound per kg of body weight is administered. Preferable amounts include 75, 135, 175, 250, and 300 mg/m^2."

Claim 13 of Rahman recites that these amounts are to be administered at least once every 21 days. Thus, the range of 0.5 to 5.0 mg paclitaxel/kg body weight every 21 days recited by Rahman overlaps almost identically with the instant claims, particularly claims 39 and 40 which require a dose of about 1 to about 7.5 mg paclitaxel/kg body weight every month. This also reaches the time limitations of the instant claim 43 for example, which recites a single administration during the first week followed by an interval of at least one or one to three weeks without administration, and then repeating.

In summary, the liposome element of the instant claims is taught in its entirety by either of McDonald or Rahman, and the breadth of the instantly claimed dosing range is very broad,

and overlaps substantially with at least the teachings of Rahman as discussed above. Applicants argue that it is improper to rely on In re Aller because In re Aller relates only to optimization of concentration or temperature, which are parameters established in the laboratory. Applicants allege that the parameters named in the instant claims cannot be "simply deduced" in the laboratory but rather instead require extensive clinical trials in human patients both of which are financially and chronologically costly. In response, a particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). Concentration is one of the parameters explicitly discussed in Aller, and applicants concede it is a result effective variable, a point not disputed by the examiner. Moreover, Aller is not the only source of case law relied upon. In fact, MPEP § 2144.05 cites several more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Furthermore, it is not clear what distinction exists between deducing in a laboratory versus deducing in a clinic, other than potentially cost or time. Furthermore, it is submitted that one of ordinary skill in the art would immediately understand that laboratory optimization can be both very costly and very lengthy. Regardless, the examiner is unaware of any element of patentability that takes into account finance and time, particularly when this is the only element relied upon for patentability as may be the case in the instant scenario.

Finally, applicants of argue that varying parameters does not support patentability unless there is evidence that such parameters are critical. Applicants argue that concentration and time variables as claimed instantly are critical, and supply evidence in the form of an attachment relating to a poster from the 34th ESMO (European Society for Medical Oncology) Multidisciplinary Congress (Berlin 2009). Applicants indicate that the poster discloses that monthly dose administration of 2.52 mg/kg, 5.04 mg/kg, and 10.08 mg/kg, demonstrated safety and effectiveness. In response, it is noted that the data is not correlated to the claim language. For example, the data discloses the use of both paclitaxel and gemcitabine, where the instant claims require only paclitaxel. The instant claims also recite a dose, which applicants argue is critical, of 0.25 mg up to about 60 mg of paclitaxel/kg body weight. Applicant data shows success over range of only 2.52 to 10.08 mg/kg, which is a much narrower window than that claimed, Particularly considering applicants clear statements that the dosage element is critical. Finally, it is also noted that the overlap between applicants data and the disclosure of Rahman is very close, and not enough to free the claims from the cited art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 36-63, and 67-77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9, 11, 14, 18, and 20 of U.S. Patent Number 7,794,747. This rejection is repeated for the same reasons of record as set forth in the action mailed April 6, 2010, but newly applied against newly submitted claims 71-77. The rejection is reproduced below, and responses to applicant's traversal follow.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the competing claims are drawn to methods of making the liposomes and the liposomes of the instant claims. Since the competing claims describe methods of making these compounds, and since the result of In Re Ochiai is that a given compounds renders its methods of making and using obvious, the instant claims are considered to be patentably indistinct from the competing claims.

Response to Arguments

Applicants argue that the claims of US Patent Number 7,794,747 are directed to novel and nonobvious methods of making a cationic liposomal composition comprising a taxane, which is patentably distinct from the instant claims, directed to allegedly novel and nonobvious methods of treating cancer in human using liposomally encapsulated paclitaxel. In response, it is noted that the patented claims expressly recite liposomally encapsulated paclitaxel. Not just

methods of making as stated in applicants response, but rather the liposomes themselves (see claims 16 for example). Furthermore, in looking to the specification to determine what type of support exists for these compounds, and furthermore what they are useful for, which is consistent with the provision for using the specification as a dictionary for determining scope and intended use (MPEP 804), it is clear that the specification discloses that these compounds are useful in treating cancer. Accordingly, the patented claims, drawn to liposomally encapsulated paclitaxel are considered to render obvious methods of using those liposomes to treat cancer as claimed instantly.

Applicants allege that if the claims of the' 747 patent and the currently pending claims were present in the same pending application patent office would have separated them into two groups of inventions. Applicants assert that it would thus be improper to impose a double patenting rejection. In response, it is not at all clear that these claims would have been separated via restriction if they had been presented in the same application. This is pure speculation on applicants part. Furthermore, even if they were, in view of In re Ochiai it would have been appropriate to withdraw the restriction at the time of allowance, in which case there is no prohibition against double patenting. Importantly, since this argument is based purely on speculation, any answer would also be speculative; thus the premise of the argument is flawed, and any reasoning flowing from it cannot be considered dispository. The rejection is maintained accordingly.

Claims 36-63, and 67-77 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 13, 16, and 22 of

copending Application No. 12/300,448. Although the conflicting claims are not identical, they are not patentably distinct from each other because the competing claims are drawn to methods of treatment using the liposomes of the instant claims. The instant claims are considered to be patentably indistinct from the competing claims because the competing claims are broader, particularly in that the competing claims don't recite treatment and dosing regimens. However, these are considered to be obvious in view of the prior art as described above, and the competing claims are accordingly considered to be patentably indistinguishable.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicants assert that the claims in Application 12/300,448 are directed to methods of inhibiting cartilage and/or bone erosion which are alleged to be patentably distinct from the claims of the present application. No evidence or reasoning as to how this conclusion was reached have been provided. Applicants also point out that the rejection is provisional and should be withdrawn in the earlier filed application, which the present case is. This is acknowledged. However, since no argument or reasoning has been presented as to why the provisional rejection is improper, the provisional rejection is maintained.

Claims 36-63, and 67-77 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 5 and 9 of copending Application No. 12/308,748. Although the conflicting claims are not identical, they are not patentably distinct from each other because the competing claims are drawn to methods of

treatment using the liposomes of the instant claims. The instant claims are considered to be patentably indistinct from the competing claims because the competing claims are broader, particularly in that the competing claims don't recite treatment and dosing regimens. However, these are considered to be obvious in view of the prior art as described above, and the competing claims are accordingly considered to be patentably indistinguishable.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicants assert that the claims in Application 12/308,748 are directed to methods of ocular neovascularization disease which are alleged to be patentably distinct from the claims of the present application. No evidence or reasoning as to how this conclusion was reached have been provided. Applicants also point out that the rejection is provisional and should be withdrawn in the earlier filed application, which the present case is. This is acknowledged. However, since no argument or reasoning has been presented as to why the provisional rejection is improper, the provisional rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. (Doug) Schultz whose telephone number is (571)272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D. (Doug) Schultz/
Primary Examiner, Art Unit 1633